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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/549,951	03/01/2006	Paul William Richard Harris	NRNZ-01048US1	1343
66936	7590	08/17/2007		
BORSON LAW GROUP, PC 1320 WILLOW PASS ROAD SUITE 490 CONCORD, CA 94520-5232			EXAMINER JARRELL, NOBLE E	
			ART UNIT 1624	PAPER NUMBER
			MAIL DATE 08/17/2007	DELIVERY MODE PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	Application No. 10/549,951	Applicant(s) HARRIS ET AL.	
	Examiner Noble Jarrell	Art Unit 1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 13 July 2007.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-19, 23, 30-32 and 35-44 is/are pending in the application.
- 4a) Of the above claim(s) 3-5, 7, 8, 10, 15, 17, 19, 23, 30-32 and 35-44 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1, 2, 6, 9, 11-14, 16 and 18 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)                                | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                       | 5) <input type="checkbox"/> Notice of Informal Patent Application                       |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

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## DETAILED ACTION

### *Election/Restrictions*

1. Applicant's election without traverse of group I in the reply filed on 7/13/2007 is acknowledged.

### *Claim Rejections - 35 USC § 112*

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 1-2, 6, 9, 11-14, 16, and 18 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for compounds encompassed by claims 1 and 6 and their salts, does not reasonably provide enablement for hydrates of these compounds. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Applicants prepare compounds of claims 1 and 6 wherein variable X is C<sub>2</sub> and C<sub>3</sub> and their salts, but do not make hydrates of these compounds. When X is C<sub>2</sub> and C<sub>3</sub>, 7 and 8-membered rings are prepared.

The factors to be considered in determining whether a disclosure meets the enablement requirements of 35 U.S.C. 112, first paragraph, have been described in *In re Wands*, 858 F.2d 731, 8 USPQ2d 1400 (Fed. Cir., 1988). The court in *Wands* states, "Enablement is not precluded by the necessity for some experimentation, such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue', not 'experimentation'" (*Wands*, 8 USPQ2d 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations" (*Wands*, 8 USPQ2d 1404). Among these factors are: (1) the nature of the invention; (2) the breadth of the claims; (3) the state of the prior art; (4) the predictability or unpredictability of the art; (5) the relative skill of those in the art; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

Consideration of the relevant factors sufficient to establish a *prima facie* case for lack of enablement is set forth below:

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*(1) The nature of the invention and (2) the breadth of the claims:*

The claims are drawn to compounds as depicted in claims 1 and 6 and their salts. Thus, the claims taken together with the specification imply a representative number of species within the genus can be prepared.

*(3) The state of the prior art and (4) the predictability or unpredictability of the art:*

The formation of hydrates is unpredictable. Vippagunta et al. (*Advanced Drug Delivery Reviews*, **2001**, 48, 3-26) state on page 15 (under heading "3.1 Introduction to solvates and hydrates"): It has been estimated that approximately one-third of the pharmaceutically active substances are capable of forming crystalline hydrates. The water molecule, because of its small size, can easily fill structural voids ... The mere presence of water in a system is not sufficient reason to expect hydrate formation, because some compounds, though they are soluble in water, do not form hydrates." Under section 3.4 (page 18), it is further stated "predicting the formation of solvates or hydrates of a compound and the number of molecules of water or solvent incorporated into the crystal lattice is complex and difficult. Each solid compound responds uniquely to the possible formation of solvates or hydrates and hence generalizations cannot be made for a series of related compounds."

*(5) The relative skill of those in the art:*

One of ordinary skill in the art is familiar with the preparation of compounds of claims 1 and 6.

*(6) The amount of direction or guidance presented and (7) the presence or absence of working examples:*

The specification has provided guidance for preparation of compounds in claims 1 and 6, wherein variable X is C<sub>2</sub> and C<sub>3</sub>, and their salts.

However, the specification does not provide guidance for the formation of hydrates of compounds of claims 1 and 6. There is also no guidance provided for the preparation of compounds of claims 1, 2 and 6 where variable X is C<sub>0</sub>. If X is C<sub>0</sub>, the ring becomes 5-membered. Applicants have not shown in any of

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the synthetic examples that they can prepare examples of the compounds in claims 1, 2 and 6, where variable X is C<sub>0</sub>.

*(8) The quantity of experimentation necessary:*

Considering the state of the art as discussed by the references above, particularly with regards to claims 1-2, 6, 9, 11-14, 16, and 18 and the high level of unpredictability in the art as evidenced therein, and the lack of guidance provided in the specification, one of ordinary skill in the art would be burdened with undue experimentation to practice the invention commensurate in the scope of the claims.

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claim 6 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Variable R as defined is not in the claimed structure and variable R<sup>1</sup> in the structure is not defined in the claim text. Applicant has failed to particularly point out the identity of the compound claimed because the structure contains an undefined variable (variable R<sup>1</sup>) and the text of the claim defines a variable that is not found in the structure (variable R).

***Claim Objections***

6. Claims 11-14 are objected to because of the following informalities: they contain non-elected subject material. Formula 3 is not encompassed within the elected group. Appropriate correction is required.

***Claim Rejections - 35 USC § 102***

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

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7. Claims 1-2 are rejected under 35 U.S.C. 102(a) as being anticipated by Roy et al. (*Journal of Peptide Research*, **2002**, 60, 198-214). Roy et al. report structures 8 (RN 518027-76-4) and 10 (RN 518027-78-6) on page 200. These structures are shown below for applicants' convenience.

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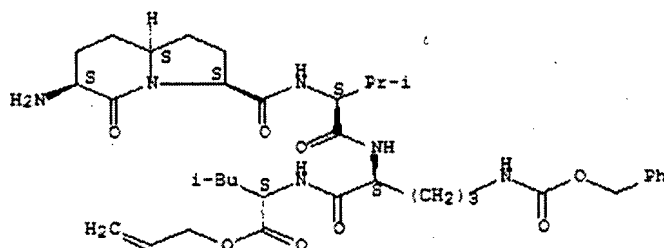
RN 518027-76-4 HCAPLUS  
 CN L-Leucine, N-[[[(3S,6S,8aS)-6-aminooctahydro-5-oxo-3-indolizinyllcarbonyl]-  
 L-valyl-N5-[(phenylmethoxy)carbonyl]-L-ornithyl-, 2-propenyl ester,  
 mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 518027-75-3

CMF C36 H54 N6 O8

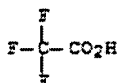
Absolute stereochemistry.



CM 2

CRN 76-06-1

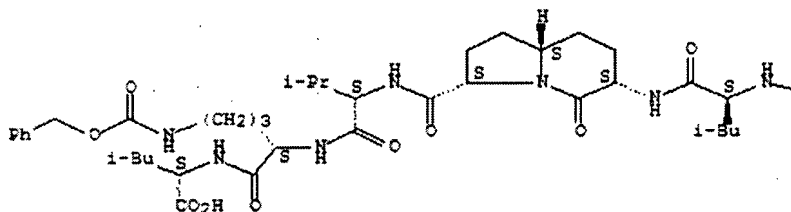
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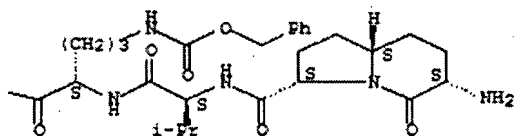
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 L-valyl-N5-[(phenylmethoxy)carbonyl]-L-ornithyl-L-leucyl-(3S,6S,8aS)-6-  
 aminooctahydro-5-oxo-3-indolizinecarbonyl-L-valyl-N5-  
 [(phenylmethoxy)carbonyl]-L-ornithyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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Both of these structures anticipate claim 1 because X is CH<sub>2</sub> in both structures, variable R<sup>2</sup> is isopropyl (alkyl), and variable R<sup>1</sup> is -C(O)NR'R', where each instance of R' is substituted alkyl. Thus, claims 1-2 are anticipated by Roy et al.

***Allowable Subject Matter***

8. No claims are allowed.
9. The elected species is considered novel.
10. The following is a statement of reasons for the indication of allowable subject matter: the closest prior art is reported by Roy et al. (discussed under 102(a)). Structures 8 and 10 (shown above) do not the limitations of claims 9, 11-14, 16, and 18. The structures do not meet the limitations of claim 9 because R<sup>1</sup> and R<sup>2</sup> are isopropyl and substituted alkyl, respectively. Claims 11 and 12 are not anticipated because R<sup>3</sup> is H, instead of methyl or allyl, respectively. Claims 13 and 14 are not anticipated because X is CH<sub>2</sub>, compared to -(CH<sub>2</sub>)<sub>3</sub>- and -(CH<sub>2</sub>)<sub>2</sub>-, respectively. Claim 16 is not anticipated because X is CH<sub>2</sub>, not -CH<sub>2</sub>-CH=CH-. Claim 18 is not anticipated because variables R<sup>1</sup>, R<sup>2</sup>, and X are isopropyl, substituted alkyl, and CH<sub>2</sub>, respectively. None of these groups meet the limitations of claim 18.

***Conclusion***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Noble Jarrell whose telephone number is (571) 272-9077. The examiner can normally be reached on M-F 7:30 A.M - 6:00 P.M. EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mr. James O. Wilson can be reached on (571) 272-0661. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

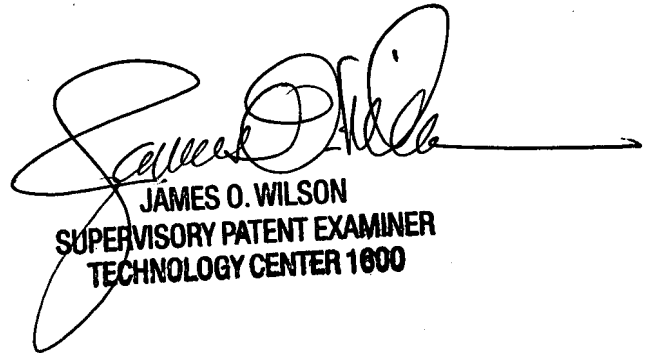


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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Noble Jarrell /NJ/

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